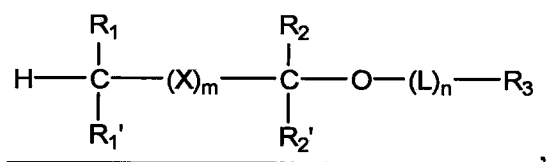


# IN THE CLAIMS

Please amend claims 1, 5, 22-24, 27, and 39-43 as shown below. The following listing of the claims replacing the previous claims.

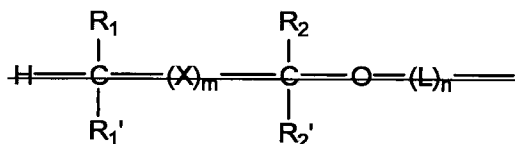
1. (Currently amended) A method for treating a pathological condition of ocular tissue, comprising contacting a therapeutically active complex with ocular tissue, wherein the complex has the structure I:



I

~~is formed by covalently attaching a moiety to a therapeutically active agent~~

wherein the pathological condition is selected from a the group consisting of macular degeneration, eye trauma, a pre-existing retinal detachment, ocular proliferative or vascular diseases, or diseases of elevated intraocular pressure or inflammation, ~~with the further proviso that the moiety is selected from a group consisting of sulfates, sulfonates, phosphates, lipids, phospholipids, carboxylates, sulfosuccinates, arginine esters, cholesterol esters, carbamates, carbonates, ketals, and the moiety having structure (I):~~



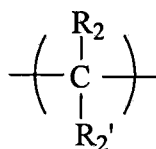
(I)

wherein in structure I:

each of  $R_1$  and  $R_1'$  is independently selected from a the group consisting of  $-H$ , an optionally substituted  $-O(C_1-C_{24})alkyl$ ,  $-O(C_1-C_{24})alkenyl$ ,  $-O(C_1-C_{24})acyl$ ,  $-S(C_1-C_{24})alkyl$ ,  $-S(C_1-C_{24})alkenyl$ , and  $-S(C_1-C_{24})acyl$ , wherein at least one of  $R_1$  and  $R_1'$  is not  $-H$ , and wherein the alkenyl or acyl optionally has between 1 and 6 double bonds,

each of  $R_2$  and  $R_2'$  is independently selected from a the group consisting of  $-H$ , an optionally substituted  $-O(C_1-C_7)alkyl$ ,  $-O(C_1-C_7)alkenyl$ ,  $-S(C_1-C_7)alkyl$ ,  $-S(C_1-C_7)alkenyl$ ,  $-O(C_1-C_7)acyl$ ,  $-S(C_1-C_7)acyl$ ,  $-N(C_1-C_7)acyl$ ,  $-NH(C_1-C_7)alkyl$ ,  $-N((C_1-C_7)alkyl)_2$ , oxo, halogen,  $-NH_2$ ,  $-OH$ , and  $-SH$ ;

X is



L is selected from a the group consisting of a valence bond and a bifunctional linking group of the formula  $-J-(CR_2)_t-G-$ , wherein t is an integer having the value between 1 and 24, each of J and G is independently selected from a the group consisting of  $-O-$ ,  $-S-$ ,  $-C(O)O-$ , and  $-NH-$ , and R is selected from a the group consisting of  $-H$ , substituted or unsubstituted alkyl, and alkenyl;

$R_3$  is a phosphate or phosphonate derivative of a therapeutically active agent;

m is an integer having the value between 0 and 6; and

n is 0 or 1,

thereby treating the pathological condition.

2-4. (Canceled).

5. (Currently amended) The method of claim 1, wherein m is selected from a the group consisting of 0, 1, or 2.

6. (Previously presented) The method of claim 1, wherein m is 1.

7. (Original) The method of claim 1, wherein the complex has a particle size from about 10 nm up to 100,000 nm.

8. (Original) The method of claim 1, wherein the complex has a particle size from about 500 nm up to 100,000 nm.

9. (Original) The method of claim 1, wherein the complex has a particle size from about 500 nm up to about 50,000 nm.

10. (Original) The method of claim 1, wherein the complex is in a slurry comprising amorphous forms and crystalline forms.

11. (Original) The method of claim 1, wherein the complex is in substantially crystalline form.

12. (Original) The method of claim 1, wherein the complex is in substantially amorphous form.

13. (Canceled).

14. (Original) The method of claim 1, wherein the therapeutically active agent is an antiviral nucleoside.

15. (Original) The method of claim 14, wherein the antiviral nucleoside is adefovir, ganciclovir, cidofovir, cyclic cidofovir, or tenofovir.

16. (Previously presented) The method of claim 14, wherein the antiviral nucleoside is a derivative of azidothymidine.

17. (Original) The method of claim 1, wherein the therapeutically active agent is an anti-neoplastic nucleoside.

18. (Original) The method of claim 17, wherein the therapeutically active agent is a derivative of cytosine arabinoside, gemcitabine, 5-fluorodeoxyuridine riboside, 5-fluorodeoxyuridine deoxyriboside, 2-chlorodeoxyadenosine, fludarabine, or 1- $\beta$ -D-arabinofuranosyl-guanine.

19. (Original) The method of claim 1, wherein the therapeutic agent is an antibody or a fragment thereof.

20. (Original) The method of claim 19, wherein the antibody is a polyclonal, a monoclonal, a chimeric, a single chain, or a humanized antibody.

21. (Original) The method of claim 19, wherein the antibody is a Fab fragment.

22. (Currently amended) ~~The A method of claim 1 for treating a pathological condition of ocular tissue, comprising administering to a subject in need thereof an effective amount of at least one complex of a therapeutically active agent, wherein the therapeutically active complex comprises particles having size between about 10 nm and about 100,000 nm, thereby treating the pathological condition, wherein the pathological condition is selected from a group consisting of macular degeneration, eye trauma, a pre-existing retinal detachment, ocular proliferative or vascular diseases, or diseases of elevated intraocular pressure or inflammation.~~

23. (Currently amended) A method for the slow-release delivery of a therapeutically active agent complex of claim 1 to ocular tissue, comprising contacting the ocular tissue with a complex of a therapeutically active agent, wherein the complex comprises particles having size between about 10 nm and about 100,000 nm, thereby

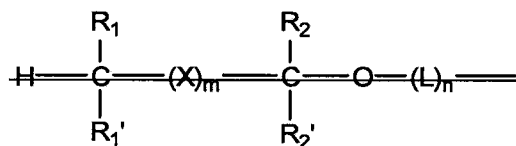
delivering a slow-release therapeutically active agent to ocular tissue, ~~wherein the delivery of the agent is provided for the treatment or prevention of a pathological condition selected from a group consisting of macular degeneration, eye trauma, a pre-existing retinal detachment, ocular proliferative or vascular diseases, or diseases of elevated intraocular pressure or inflammation.~~

24. (Currently amended) A method for increasing residence time of a therapeutically active agent in ocular tissue, comprising forming the therapeutically active complex ~~covalently attaching the moiety of claim 1~~ 22 to the therapeutically active agent to form a complex comprising particles having size between about 10 nm and about 100,000 nm, and contacting the therapeutically active complex with ocular tissue, thereby increasing residence time of a the therapeutically active agent in ocular tissue.

25. (Previously presented) The method of any one of claims 1, 22, or 23, wherein the pathological condition is selected from a group consisting of macular degeneration and eye trauma.

26. (Previously presented) The method of any one of claims 1, 22, or 23, wherein the pathological condition is eye trauma.

27. (Currently amended) A The method for treating a pathological condition of ocular tissue of claim 1, ~~comprising contacting a therapeutically active complex with ocular tissue, wherein the complex is formed by covalently attaching a moiety to a therapeutically active agent is selected from a the group consisting of adefovir, cidofovir, cyclic cidofovir, tenofovir, a derivative of azidothymidine, an anti-neoplastic nucleoside, and an antibody or a fragment thereof, thereby treating the condition, and wherein the pathological condition is selected from a the group consisting of macular degeneration, eye trauma, or and a pre-existing retinal detachment, with the further proviso that the moiety is selected from a group consisting of sulfates, sulfonates, phosphates, lipids, phospholipids, carboxylates, sulfosuccinates, arginine esters, cholesterol esters, carbamates, carbonates, ketals, and the moiety having structure (I):~~



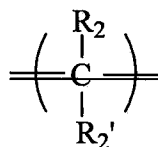
(I)

wherein:

each of R<sub>1</sub> and R<sub>1</sub>' is independently selected from a group consisting of H, an optionally substituted O(C1-C24)alkyl, O(C1-C24)alkenyl, O(C1-C24)acyl, S(C1-C24)alkyl, S(C1-C24)alkenyl, and S(C1-C24)acyl, wherein at least one of R<sub>1</sub> and R<sub>1</sub>' is not H, and wherein the alkenyl or acyl optionally has between 1 and 6 double bonds;

each of R<sub>2</sub> and R<sub>2</sub>' is independently selected from a group consisting of H, an optionally substituted O(C1-C7)alkyl, O(C1-C7)alkenyl, S(C1-C7)alkyl, S(C1-C7)alkenyl, O(C1-C7)acyl, S(C1-C7)acyl, N(C1-C7)acyl, NH(C1-C7)alkyl, N((C1-C7)alkyl)<sub>2</sub>, oxo, halogen, NH<sub>2</sub>, OH, and SH;

X is



L is selected from a group consisting of a valence bond and a bifunctional linking group of the formula J-(CR<sub>2</sub>)<sub>t</sub>-G, wherein t is an integer having the value between 1 and 24, each of J and G is independently selected from a group consisting of O, S, C(O)O, and NH, and R is selected from a group consisting of H, substituted or unsubstituted alkyl, and alkenyl;

m is an integer having the value between 0 and 6; and

———n is 0 or 1.

28. (Previously presented) The method of claim 27, wherein m is selected from a group consisting of 0, 1, or 2.

29. (Previously presented) The method of claim 27, wherein m is 1.

30. (Previously presented) The method of claim 27, wherein the complex has a particle size from about 10 nm up to 100,000 nm.

31. (Previously presented) The method of claim 27, wherein the complex has a particle size from about 500 nm up to 100,000 nm.

32. (Previously presented) The method of claim 27, wherein the complex has a particle size from about 500 nm up to about 50,000 nm.

33. (Previously presented) The method of claim 27, wherein the complex is in a slurry comprising amorphous forms and crystalline forms.

34. (Previously presented) The method of claim 27, wherein the complex is in substantially crystalline form.

35. (Previously presented) The method of claim 27, wherein the complex is in substantially amorphous form.

36. (Previously presented) The method of claim 27, wherein the an anti-neoplastic nucleoside is a derivative of cytosine arabinoside, gemcitabine, 5-fluorodeoxyuridine riboside, 5-fluorodeoxyuridine deoxyriboside, 2-chlorodeoxyadenosine, fludarabine, or 1- $\beta$ -D-arabinofuranosyl-guanine.

37. (Previously presented) The method of claim 27, wherein the antibody is a polyclonal, a monoclonal, a chimeric, a single chain, or a humanized antibody.

38. (Previously presented) The method of claim 37, wherein the antibody is a Fab fragment.

39. (Currently amended) ~~A The method for treating a pathological condition of ocular tissue of claim 27, comprising administering to a subject in need thereof an effective amount of at least one complex of a therapeutically active agent, wherein the therapeutically active complex comprises particles having size between about 10 nm and about 100,000 nm, thereby treating the pathological condition, wherein the pathological condition is selected from a group consisting of macular degeneration, eye trauma, or a pre-existing retinal detachment, with the further proviso that the therapeutically active agent is selected from a group consisting of adefovir, cidofovir, cyclic cidofovir, tenofovir, a derivative of azidothymidine, an anti-neoplastic nucleoside, and an antibody or a fragment thereof.~~

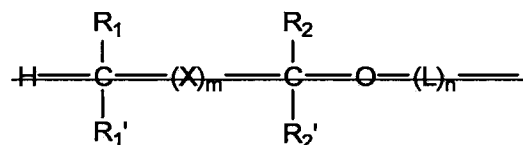
40. (Currently amended) A method for the slow-release delivery of a the therapeutically active agent of claim 27 to ocular tissue, comprising contacting the ocular tissue with a complex of a the therapeutically active agent, wherein the complex comprises particles having size between about 10 nm and about 100,000 nm, thereby delivering a ~~slow-release~~ the therapeutically active agent to ocular tissue, wherein the delivery of the agent is provided for the treatment or prevention of a pathological condition selected from a the group consisting of macular degeneration, eye trauma, ~~or and~~ a pre-existing retinal detachment, ~~with the further proviso that the therapeutically active agent is selected from a group consisting of adefovir, cidofovir, cyclic cidofovir, tenofovir, a derivative of azidothymidine, an anti-neoplastic nucleoside, and an antibody or a fragment thereof.~~

41. (Currently amended) A method for increasing residence time of a therapeutically active agent in ocular tissue, comprising forming the therapeutically active complex ~~covalently attaching the moiety of claim 1~~ 27 to the therapeutically active agent to form a complex comprising particles having size between about 10 nm and about



100,000 nm, and contacting the therapeutically active complex with ocular tissue, thereby increasing residence time of a the therapeutically active agent in ocular tissue, ~~with the further proviso that the therapeutically active agent is selected from a group consisting of adefovir, cidofovir, cyclic cidofovir, tenofovir, a derivative of azidothymidine, an anti-neoplastic nucleoside, and an antibody or a fragment thereof.~~

42. (Currently amended) A The method of claim 1 for treating a pathological condition of ocular tissue, comprising contacting a therapeutically active complex with ocular tissue, wherein the complex is formed by covalently attaching a moiety to a therapeutically active agent, wherein the pathological condition is selected from a the group consisting of macular degeneration, ocular proliferative or vascular diseases, or and diseases of elevated intraocular pressure or inflammation, with the further proviso that the moiety is selected from a group consisting of sulfates, sulfonates, phosphates, lipids, phospholipids, carboxylates, sulfosuccinates, arginine esters, cholesterol esters, carbamates, carbonates, ketals, and the moiety having structure (I):



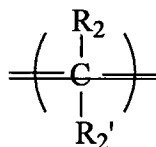
(I)

~~wherein:~~

~~each of R<sub>1</sub> and R<sub>1</sub>' is independently selected from a group consisting of H, an optionally substituted O(C<sub>1</sub>-C<sub>24</sub>)alkyl, O(C<sub>1</sub>-C<sub>24</sub>)alkenyl, O(C<sub>1</sub>-C<sub>24</sub>)acyl, S(C<sub>1</sub>-C<sub>24</sub>)alkyl, S(C<sub>1</sub>-C<sub>24</sub>)alkenyl, and S(C<sub>1</sub>-C<sub>24</sub>)acyl, wherein at least one of R<sub>1</sub> and R<sub>1</sub>' is not H, and wherein the alkenyl or acyl optionally has between 1 and 6 double bonds,~~

~~each of R<sub>2</sub> and R<sub>2</sub>' is independently selected from a group consisting of H, an optionally substituted O(C<sub>1</sub>-C<sub>7</sub>)alkyl, O(C<sub>1</sub>-C<sub>7</sub>)alkenyl, S(C<sub>1</sub>-C<sub>7</sub>)alkyl, S(C<sub>1</sub>-C<sub>7</sub>)alkenyl, O(C<sub>1</sub>-C<sub>7</sub>)acyl, S(C<sub>1</sub>-C<sub>7</sub>)acyl, N(C<sub>1</sub>-C<sub>7</sub>)acyl, NH(C<sub>1</sub>-C<sub>7</sub>)alkyl, N((C<sub>1</sub>-C<sub>7</sub>)alkyl)<sub>2</sub>, oxo, halogen, NH<sub>2</sub>, OH, and SH;~~

~~X is~~



~~L is selected from a group consisting of a valence bond and a bifunctional linking group of the formula J (CR<sub>2</sub>)<sub>t</sub> G, wherein t is an integer having the value between 1 and 24, each of J and G is independently selected from a group consisting of O, S, C(O)O, and NH, and R is selected from a group consisting of H, substituted or unsubstituted alkyl, and alkenyl;~~

~~m is an integer having the value between 0 and 6; and~~

~~n is 0 or 1.~~

43. (Currently amended) The method of claim 42, wherein m is selected from a the group consisting of 0, 1, or 2.

44. (Previously presented) The method of claim 42, wherein m is 1.

45. (Previously presented) The method of claim 42, wherein the complex has a particle size from about 10 nm up to 100,000 nm.

46. (Previously presented) The method of claim 42, wherein the complex has a particle size from about 500 nm up to 100,000 nm.

47. (Previously presented) The method of claim 42, wherein the complex has a particle size from about 500 nm up to about 50,000 nm.

48. (Previously presented) The method of claim 42, wherein the complex is in a slurry comprising amorphous forms and crystalline forms.

49. (Previously presented) The method of claim 42, wherein the complex is in substantially crystalline form.

50. (Previously presented) The method of claim 42, wherein the complex is in substantially amorphous form.

51. (Previously presented) The method of claim 42, wherein the therapeutically active agent is an antiviral nucleoside.

52. (Previously presented) The method of claim 51, wherein the antiviral nucleoside is adefovir, ganciclovir, cidofovir, cyclic cidofovir, or tenofovir.

53. (Previously presented) The method of claim 51, wherein the antiviral nucleoside is a derivative of azidothymidine.

54. (Previously presented) The method of claim 42, wherein the therapeutically active agent is an anti-neoplastic nucleoside.

55. (Previously presented) The method of claim 54, wherein the therapeutically active agent is a derivative of cytosine arabinoside, gemcitabine, 5-fluorodeoxyuridine riboside, 5-fluorodeoxyuridine deoxyriboside, 2-chlorodeoxyadenosine, fludarabine, or 1- $\beta$ -D-arabinofuranosyl-guanine.

56. (Previously presented) The method of claim 42, wherein the therapeutic agent is an antibody or a fragment thereof.

In Re Application Of:

Hostetler et al.

Application No.: 10/770,885

Filed: February 2, 2004

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PATENT

Attorney Docket No. UCSD1480-1

57. (Previously presented) The method of claim 56, wherein the antibody is a polyclonal, a monoclonal, a chimeric, a single chain, or a humanized antibody.

58. (Previously presented) The method of claim 56, wherein the antibody is a Fab fragment.

59-61. (Canceled).